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Clinical and Angiographic Outcomes after Contemporary Extraplaque Compared to Intraplaque Recanalization of Chronic Total Occlusion: a 6-Month Follow-up Observational Study

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SOUHRN

Cíl: Stále častější používání subintimální a subadventiciální rekanalizace (extraplaque, EP) strategií bylo spojeno se stále úspěšnější rekanalizací chronického totálního uzávěru (chronic total occlusion, CTO) koronárních tepen. Současné techniky EP nahradily předchozí techniky disekce a „reentry" a prokázaly střednědobé výsledky srovnatelné s výsledky rekanalizace skrze plát (intraplaque, IP). Nyní je třeba klinické a angiografické výsledky vyhodnotit. Cílem této studie bylo posoudit klinické a angiografické výsledky různých technik perkutánní koronární intervence (PCI) v léčbě CTO.
Metody: Provedli jsme prospektivní, observační, analytickou, monocentrickou studii, do níž bylo zařazeno 50 po sobě následujících pacientů s úspěšně provedenou PCI v léčbě CTO. Uvedené odlišné přístupy PCI (EP vs. IP) byly použity podle úsudku operatéra. Primárním sledovaným parametrem byly klinické a angiografické výsledky použité techniky PCI po šesti měsících od daného výkonu.
Výsledky: U 50 po sobě následujících pacientů byla v 51 případech CTO koronární tepny provedena úspěšná PCI. V 15 případech byla použita EP technika a v 36 byla použita IP technika. Po šesti měsících sledování byly u všech pacientů zhodnoceny klinické a angiografické výsledky. Rekanalizace cílové tepny byla neúspěšná (target vessel failure, TVF) u 23,5 % všech pacientů, přičemž těchto pacientů bylo více ve skupině s EP; rozdíl však nedosáhl statistické významnosti (26,6 % vs. 22,2 %; $p = 0,73$).
Závěry: Zprůchodnění CTO technikou EP – oproti technice IP – je spojeno se statisticky nevýznamným rozdílem v TVF.

ABSTRACT

Aim: The expanding utilization of extraplaque (EP) strategies has led to increasing success rates in coronary chronic total occlusion (CTO) recanalization. The contemporary EP techniques have replaced the precedent dissection and reentry techniques and have shown mid-term outcomes comparable to intraplaque (IP) approaches. Clinical and angiographic outcomes need to be evaluated. The aim of this study was to assess clinical and angiographic outcomes across different CTO-PCI techniques.
Methods: This was a prospective, observational, analytic, single-center study recruiting 50 consecutive patients who underwent successful CTO PCI. The CTO PCI technique (EP vs. IP) was according to the operator's discretion. The primary endpoint was contrasting the impact of the PCI technique on the clinical and angiographic outcomes, 6 months after the index PCI.
Results: Fifty consecutive patients had successful PCI to 51 CTO coronary vessels. EP and IP techniques were used in 15 and 36 CTOs, respectively. At 6 months, clinical and angiographic follow-ups were completed for all patients. Target vessel failure (TVF) occurred in 23.5% of all patients with a numerically higher rate in the EP compared to the IP technique but without achieving statistical significance (26.6% vs. 22.2%; $p = 0.73$).
Conclusions: CTO recanalization using EP techniques is associated with non-significant difference in TVF compared to IP techniques.

Keywords:
Chronic total occlusion
Extraplaque
Intraplaque

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Introduction

In interventional cardiology, treating chronic total occlusions (CTO) with percutaneous coronary intervention (PCI) has consistently been a distinct challenge.[1–3] CTO PCI procedures are inclined to have lower success rates and a higher risk of complications compared to non-CTO PCI.[4,5] Historically, antegrade wire escalation (AWE) served as the primary approach for CTO PCI; however, early reports showed success rates of only about 80%.[6] Moreover, the AWE technique often proves unsuccessful in cases involving highly complex, tortuous, and/or long CTO lesions.[6,7]

By virtue of improved operator expertise, ongoing technological progress, and the introduction of new techniques, modern CTO PCI now achieves success rates above 95%, while also expanding the range of complex CTOs that can be treated effectively.[8,9] A key driver in this progress has been the incorporation of multiple recanalization techniques beyond AWE. Contemporary CTO PCI procedures use a hybrid method, customizing the recanalization strategy to address the unique anatomical difficulties of each lesion.[9–11] This can include antegrade and retrograde methods, combining the traditional intra-plaque (IP) technique or sometimes an extra-plaque (EP) approach, with operators often switching between these various techniques when dealing with complex CTOs.[9]

In fact, the use of extra-plaque (EP) strategies, including antegrade dissection re-entry (ADR) and reverse controlled antegrade-retrograde tracking (CART), has greatly enhanced the ability to navigate uncrossable CTO plaques and re-enter the true lumen, thereby markedly improving the success rates of CTO PCI.[12] This has enabled interventionalists to tackle more complex CTOs, broadening the range of difficult lesions they can treat.[3] Nevertheless, employing EP techniques brings up concerns about long-term vascular healing. Having a portion of the neo-lumen located within the extra-plaque space could potentially influence stent endothelialization and neo-intimal formation, which may ultimately affect long-term vessel openness and clinical results.[13] As a result, the growing use of EP strategies creates an urgent need to thoroughly understand their long-term effects on CTO PCI outcomes.

Methods

This was a prospective, observational, single-center study, that was conducted in a high-volume CTO cardiac center through February 2024 to March 2025. The study protocol was registered and approved by the institutional research ethics committee and all patients provided written informed consent prior to recruitment. The study aimed to explore the mid-term clinical and angiographic outcomes. Selection of the CTO canalization strategy (antegrade vs. retrograde and intraplaque vs. extraplaque) was according to the operator's judgement of the CTO anatomical characteristics, in lieu of the Global CTO crossing algorithm.[8] According to the institutional practice, utilization of intravascular imaging (IVUS or OCT) in guiding CTO recanalization is liberal.

Study population

CTO PCI was primarily indicated for patients experiencing angina (or equivalent symptoms) that persisted despite optimal medical treatment, along with confirmed evidence of viable myocardium in the affected territory. The inclusion criteria included: (1) age between 18 and 80 years; (2) approval to participate via written informed consent; (3) CTO involving a native segment in a major epicardial coronary vessel, (4) presence of angina symptoms in addition to documented viability of the target myocardial territory by either cardiac magnetic resonance imaging (CMR) or myocardial perfusion imaging (MPI); and (5) successful PCI of the CTO vessel by ≥1 new generation DES. Exclusion criteria included: (1) CTO lesions in surgical grafts or in previously stented segments (in-stent CTO); (2) chronic kidney disease CKD with estimated glomerular filtration rate ≤ 45 ml/min/m^2; and (3) permanent indication for oral anticoagulant (OAC) therapy.

Study workup and CTO recanalization protocol

The PCI was conducted using standard techniques. Dual injection angiography was routinely used at the beginning to thoroughly assess the CTO anatomy. Following this, the J-CTO and PROGRESS CTO scores were calculated.[1,14] Technical success was defined as successful restoration of TIMI III antegrade flow with residual stenosis ≤30%,[15] while procedural success was defined as technical success and discharge of the patient without in-hospital major adverse cardiovascular events (MACE) that included death, myocardial infarction, stroke or target vessel revascularization.[10,15–17]

Clinical and angiographic follow-up

Patients were followed up clinically for 6 months, then underwent control angiography. Through the follow-up period, freedom from MACE, angina, heart failure, re-hospitalization, and urgent unplanned revascularization were periodically evaluated. Target vessel failure (TVF) was defined as new angiographic >50% diameter stenosis in the treated vessel. Ischemia-driven target vessel revascularization (TVR) was contemplated when encountering a TVF associated with either clinical angina or physiologic evidence of a significant amount of ischaemia.

Study endpoints

The study's endpoint was the freedom from MACE and ischemia-driven target vessel revascularization (TVR) at 6 months.

Statistical analysis

After tabulation and verification of the data, statistical analysis was conducted using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY) and MedCalc Statistical Software, Version 20.1 (MedCalc Software Ltd., Ostend, Belgium). Data were presented as mean ± standard deviation, median (25th–75th percentile), or frequency (percentage), as appropriate. Between-group comparisons were conducted using the Student's t-test, McNemar's test, or Fisher's exact test. To assess predictors of TVF, a receiver operating characteristic (ROC) curve was constructed for relevant parameters. A p-value ≤0.05 was considered statistically significant.

Results

During the study period, from February 2024 to March 2025, 78 CTO procedures were performed with an overall technical success of 92%. Fifty patients met the eligibility criteria (who had 51 CTO lesions) and comprised the study group, while 19 patients had in-stent CTO and 9 ended with investment procedure, hence were excluded. The study flowchart is illustrated in **Figure 1**. The mean age was 57.7 ± 8 years and 35 (68.6%) were males. The baseline characteristics and clinical data of the whole group and contrasting EP vs. IP recanalization subgroups are outlined in **Table 1**.

The left anterior descending (LAD) artery was the CTO vessel in 24 patients (47%). The mean J-CTO score was 2.5 ± 1 and the mean Progress CTO score was 1.7 ± 0.8. The successful strategy was AWE in 28 (54.9%), RWE in 8 (15.7%), ADR in 4 (7.8%), and RDR in 11 (21.6%). Pre-stenting IVUS was available in 31 (60.7%) of the procedures, with significantly higher utilization in the EP vs. the IP recanalization groups, 13 (86.7%) vs. 18 (51.4%), respectively, with $p = 0.019$. The angiographic and procedural data are summarized in **Table 2**.

All 50 patients were followed up clinically for 6 months post-PCI without reporting any MACE. On the control coronary angiography, TVF (defined as new angiographic diameter stenosis of >50%) was met in 12 (23.5%) of the 51 recanalized CTOs. Of these, 8 had associated evidence of ischemia and underwent TVR which was comparable between the 2 strategies. On the other hand, discretionary optimization was decided by the operator in other 2 patients, 1 in each group. These findings are detailed in **Table 3**.

Predictors for TVF were sought from the angiographic parameters. Only the stented length was the significant predictor in univariate regression analysis. For the stented length, the ROC-curve analysis yielded a cut-off value of >70 mm as a significant predictor for TVF with a sensitivity of 75 % and specificity of 74% to predict target vessel failure TVF ($p = 0.0117$) (see **Figure 2**). The central illustration of the study outcomes is represented in **Figure 3**.

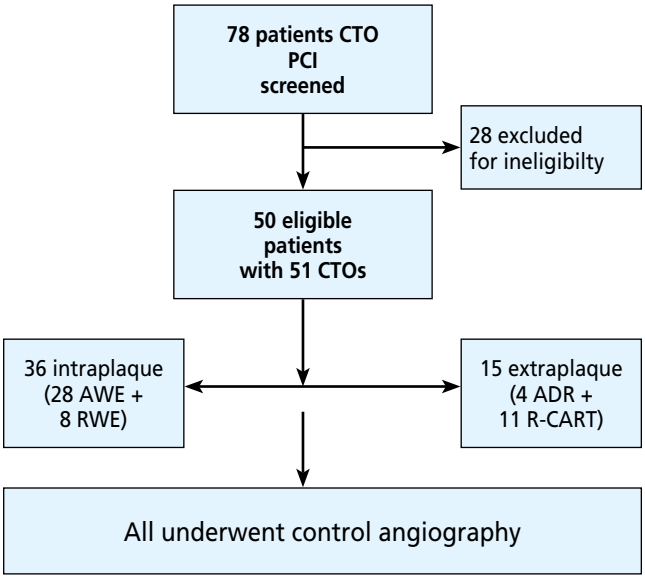


Fig. 1 – Study flow chart. ADR – antegrade dissection re-entry; AWE – antegrade wire escalation; CTO – chronic total occlusion; NIHS – neo-intimal healing score; PCI – percutaneous coronary intervention; R-CART – reverse controlled antegrade-retrograde tracking; RWE – retrograde wire escalation; TVR – target vessel revascularization.

Table 1 – Baseline characteristics of the whole study group and the differences between intraplaque vs. extraplaque recanalization subgroups

	All patients (N = 50)	EP group (N = 15)	IP group (N = 35[$])	*p*-value[*]
Age (years)	58 ± 8	53 ± 9	57 ± 8	0.009
Weight (kg)	84 ± 17	87.7 ± 16.7	83.8 ± 16.8	0.29
Height (meters)	1.66 ± 9	1.69 ± 9.3	1.66 ± 9.1	0.12
BMI (mg/m^2)	30.2 ± 6	30.5 ± 5	30.2 ± 5.9	0.87
Diabetes mellitus	33 (66%)	9 (60%)	24 (66.7%)	0.75
Hypertension	34 (68%)	7 (46.7%)	27 (75%)	0.10
Current smoking	28 (56%)	10 (66.7%)	18 (50%)	0.36
Dyslipidemia	29 (58%)	9 (64.3%)	20 (55.6%)	0.75
Family history of premature CAD	3 (6%)	2 (13.3%)	1 (2.9%)	0.21
Prior MI	22 (44%)	5 (33.3%)	17 (47.2%)	0.53
Prior CABG	4 (8%)	3 (20%)	1 (2.8%)	0.07
Prior PCI	28 (56%)	10 (66.7%)	18 (50%)	0.36

BMI – body mass index; CABG – coronary artery bypass graft surgery; CAD – coronary artery disease; EP – extraplaque; IP – intraplaque; MI – myocardial infarction; PCI – percutaneous coronary intervention.
Data represented as mean ± standard deviation or frequency (percentage) as appropriate.
[*] Denotes EP versus IP recanalization groups.
[$] Number of patients but counting for 36 CTOs.

Table 2 – Angiographical and procedural characteristics

	All CTO vessels (N = 51)	EP group (N = 15)	IP group (N = 36)	*p*-value
CTO vessel:				0.021
LAD	24 (47%)	3 (20%)	21 (58%)	
LCX	4 (8%)	1 (7%)	3 (8%)	
RCA	23 (45%)	11 (73%)	12 (33%)	
Ambiguous proximal cap	30 (59%)	9 (60%)	22 (58%)	0.7
CTO length (mm)	35.9 ± 24	68 ± 30	36 ± 23	0.001
J-CTO score	2.5 ± 1	2.6 ± 0.8	2.5 ± 1	0.5
PROGRESS CTO score	1.7 ± 0.8	1.7 ± 0.6	1.7 ± 0.8	0.7
Antegrade approach	32 (63%)	4 (26.7%)	28 (77.8%)	0.001
Retrograde approach	19 (37%)	11 (73.3%)	8 (22.2%)	0.001
IVUS use	31 (61%)	13 (86.7%)	18 (51.4%)	0.019
Contrast volume (ml)	300 (240–350)	320 (278–388)	300 (242–350)	0.274
Fluro time (min)	45 (23.8–69.5)	80 (59–83)	31 (23–69)	0.001
Fluro dose (Gray)	3.3 (2.3–5.6)	5.4 (3.2–6)	3 (2.3–5.6)	0.065

CTO – chronic total occlusion; EP – extraplaque; IP – intraplaque; LAD – left anterior descending; LCX – left circumflex; RCA – right coronary artery. Data represented as mean ± standard deviation, median (25^{th}–75^{th} percentile), or frequency (percentage) as appropriate.

Table 3 – Clinical and angiographic outcomes at the 6-month follow-up

	All CTO vessels (N = 51)	EP (N = 15)	IP (N = 36)	*p*-value
MACE	0	0	0	–
TVF*	12 (23.5%)	4 (26.6%)	8 (22.2%)	0.73
Ischemia-driven TVR	8 (15.7%)	2 (13.3%)	6 (16.7%)	0.45
Discretionary optimization$	2 (25.4%)	1 (6.7%)	1 (2.8)	0.51

MACE – major adverse cardiovascular events, defined as death, myocardial infarction, stroke, urgent unplanned revascularization; TVF – target vessel failure; TVR – target vessel revascularization.
Data represented as frequency (percentage).
* Including all those who met the angiographic definition, either with or without evidence of ischemia.
$ Representing the operator's decision for optimization in the absence of evidence of ischemia, for example, a malopposed segment with 60% in-stent restenosis in proximal LAD.

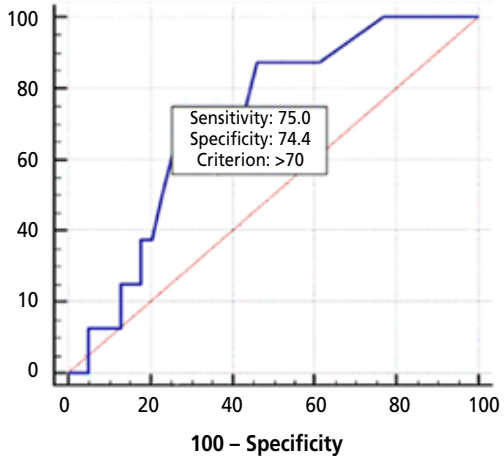
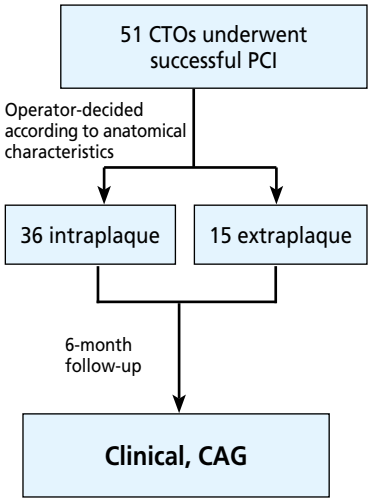


Fig. 2 – Receiver operating curve analysis for stented-segment length in predicting TVF by 6 months.

Discussion

EP recanalization has enabled the treatment of complex coronary CTOs that were previously thought unmanageable by IP techniques. With the evolution of EP techniques, the overall success rate of CTO PCI has significantly improved, extending its capabilities beyond those of traditional IP approaches.[18] However, although early EP techniques such as STAR (Subintimal Tracking and Reentry) and LAST (Limited Antegrade Subintimal Tracking) achieved high procedural success, they were associated with elevated rates of target vessel failure (TVF) over time.[19] Apparently, the extensive vascular injury caused by creating a channel outside the occluded segment triggers a robust reparative response, which is believed to contribute to restenosis and subsequent target vessel failure (TVF).[20]

Accordingly, pursuing to improve long-term patency, advancements in the techniques and armamentarium of



	Extraplaque CTO PCI		Intraplaque CTO PCI		*p*-value
CTO length (mm)	68 ± 30		36 ± 23		0.001
J-CTO score	2.6 ± 0.8		2.5 ± 1		0.5
Retrograde approach	11 (73.3%)		8 (22.2%)		0.001
Fluro time (min)	80 (59–83)		31 (23–69)		0.001
Contrast volume (ml)	320 (278–388)		300 (242–350)		0.274
Total stented length (mm)	82.2 ± 29.9		52.9 ± 23.7		0.003
TVF	4 (26.6%)		8 (22.2%)		0.33

Fig. 3 – Central illustration for the study findings. CTO – chronic total occlusion; PCI – percutaneous coronary intervention.

EP CTO PCIs aimed at minimization of the trauma/injury to the coronary vascular walls. In contemporary practice, several studies have suggested that Stingray or R-CART facilitated re-entry, which are characterized by limited and controlled EP tracking, have excellent immediate and mid-term outcomes comparable to IP procedures.[21,22] From a clinical standpoint, there are growing concerns about higher MACE rates with EP compared to IP recanalization, especially following a recent meta-analysis that reported an elevated risk of 1-year target vessel revascularization (TVR) associated with EP CTO PCI.[13]

This study aimed to prospectively evaluate the differences between modern EP and IP techniques and their respective effects on mid-term clinical and angiographic outcomes. Among the 51 CTO PCI cases analyzed, 15 were managed using EP recanalization based on specific anatomical considerations. Compared to the IP group, patients in the EP group were older, had longer CTO lesions, more frequently underwent retrograde approaches, and had a higher prevalence of prior CABG. These parameters of increased complexity in the EP group were reflected in significantly longer procedure times and greater use of IVUS, although the volume of contrast used was similar between both techniques.

It is important to consider that CTOs chosen for EP recanalization generally have more complex anatomy and involve longer stented segments than those treated with the IP method. In this study, the type of revascularization technique (EP versus IP) did not serve as a predictor for future target vessel failure. Instead, the overall length of the stented segment was linked to angiographically confirmed TVF at 6 months after the procedure.

Study limitations

This study has some limitations, including a small sample size, single-center experience, and an unblinded design. Therefore, a larger, multicenter study with blinding of the recanalization technique for the cardiologists evaluating the endpoints is warranted to minimize potential assessment bias.

Conclusions

Contemporary EP techniques, which have significantly improved CTO PCI success rates, are not associated with different rates of TVF or MACE.

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Impact on daily practice
This study compares the intraplaque and extraplaque techniques for CTO revascularization, focusing on clinical outcomes after 6 months.

Conflict of interest
There is no conflict of interest to be mentioned.

Availability of data and materials
These can be made available upon reasonable request from the corresponding author.

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None.

Authors contribution
All authors shared in the conceptualization of the study, writing and revision. The final version has been approved by all authors.

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